

AMENDMENTS TO THE CLAIMS:

Please amend claims 45 and 62, and add claims 105-110. This listing of the claims replaces all prior versions and listing of claims in the application.

LISTING OF CLAIMS:

1 – 44 Cancelled

45. (Currently Amended) A nucleic acid molecule that encodes a mutant adeno-associated virus (AAV) Rep protein that has increased activity, wherein:

increased activity of the Rep protein is manifested as an increased titer of virus at 37° C upon introduction and replication of virus ~~under standard conditions for wild type virus production~~ in a host cell that contains in its genome the nucleic acid molecule encoding the mutant Rep protein, compared to the titer of virus upon introduction and replication of a virus in a host cell containing a wild type Rep gene;

the AAV serotype is an AAV-1, AAV-2, AAV-3, AAV-3b, AAV-4 or AAV6 serotype; and

the mutation is in the corresponding position in each serotype.

46. (Previously Presented) [[A]] An isolated cell, comprising the nucleic acid molecule of claim 45.

47 - 61 Cancelled

62. (Previously Presented)) A nucleic acid molecule ~~of claim 45,~~ encoding a mutant AAV Rep protein having mutations at one or more [[of]] amino acid residues, ~~whereby the activity of the mutant Rep protein is increased as assessed by rAAV production compared to the wild type Rep protein,~~ wherein:

increased activity of the Rep protein is manifested as an increased titer of virus upon introduction and replication of virus in a host cell that contains in its genome the nucleic acid molecule encoding the mutant Rep protein, compared to the titer of virus upon introduction and replication of a virus in a host cell containing a wild type Rep gene;

the AAV serotype is an AAV-1, AAV-2, AAV-3, AAV-3b, AAV-4 or AAV6 serotype;

the mutation is in the corresponding position in each serotype;

the mutations comprise replacements of native amino acid residue(s) selected from among: T by N at position 350 of SEQ ID No. 747; T by I at position 462 of SEQ ID No. 747; P by R or L or Y at position 497 of SEQ ID No. 747; T by N at position 517 of SEQ ID No. 747; G by D or S at position 598 of SEQ ID No. 747; or V by P at position 600 of SEQ ID No. 747 or the same replacements at the corresponding positions in the other serotypes;

residue 1 corresponds to residue 1 of the Rep78 protein encoded by nucleotides 321-2186 of SEQ ID No. 746 of the AAV-2 genome; and

the listed positions reference positions in the sequence of amino acids set forth in SEQ ID NO:747 encoded by wildtype AAV-2 nucleic acid molecules set forth in SEQ ID NO:746 .

63. – 69. Cancelled.

70. (Original) A recombinant AAV, comprising the nucleic acid molecule of claim 62.

71. – 77. Cancelled.

78. (Previously Presented) [[A]] An isolated cell, comprising the recombinant AAV of claim 70.

79- 93. Cancelled.

94. (Previously presented) The nucleic acid of claim 62, wherein the Rep protein is Rep 78, Rep 68, Rep 52 or Rep 40.

95. Cancelled.

96. (Previously Presented) A nucleic acid molecule of claim 62, wherein:
the nucleic acid molecule encodes a mutant Rep protein comprising a sequence of amino acids set forth in any of SEQ ID Nos. 113-116, 213-216, 233-244, 277-280, 293, 294, 297 and 298; or

the nucleic acid molecule encode Rep proteins in any of AAV-1, AAV-2, AAV-3, AAV-3b, AAV-4, and AAV-6 containing the same replacements at the corresponding positions.

97. (Previously Presented) A nucleic acid molecule of claim 62 encoding a mutant Rep protein comprising a sequence of amino acids set forth in any of SEQ ID Nos. 113-116, 213-216, 233-244, 277-280, 293, 294, 297 and 298.

98. (Previously presented) A recombinant AAV, comprising the nucleic acid molecule of claim 45.

99. (Previously presented) A recombinant AAV, comprising the nucleic acid molecule of claim 96.

100. (Previously presented) A recombinant AAV, comprising the nucleic acid molecule of claim 97.

101. (Previously Presented) A nucleic acid molecule of claim 45, encoding a mutant AAV Rep protein having mutations at one or more amino acid residues, whereby the activity of the mutant Rep protein is increased as assessed by rAAV production compared to the wild type Rep protein,

wherein:

the mutations comprise replacements of native amino acid residue(s) selected from among: L by S at position 542 of SEQ ID No. 747; or R by S at position 548 of SEQ ID No. 747; or the same replacements at the corresponding positions in the other serotypes;

residue 1 corresponds to residue 1 of the Rep78 protein encoded by nucleotides 321-2186 of SEQ ID No. 746 of the AAV-2 genome; and

the listed positions reference positions in the sequence of amino acids set forth in SEQ ID NO:747 encoded by wildtype AAV-2 nucleic acid molecules set forth in SEQ ID NO:746.

102. (Previously Presented) A nucleic acid molecule of claim 101, wherein:

the nucleic acid molecule encode Rep proteins in any of AAV-1, AAV-2, AAV-3, AAV-3b, AAV-4, and AAV-6 containing the same replacements at the corresponding positions.

103. (Previously Presented) A recombinant AAV, comprising the nucleic acid molecule of claim 101.

104. (Previously Presented) A recombinant AAV, comprising the nucleic acid molecule of claim 102.

105. (New) A nucleic acid molecule that encodes a mutant adeno-associated virus (AAV) Rep protein that has increased activity, wherein:

increased activity of the Rep protein is manifested as an increased titer of virus upon introduction and replication of the virus in a host cell that contains in its genome the nucleic acid molecule encoding the mutant Rep protein, compared to the titer of virus upon introduction and replication of a virus in a host cell containing a wild type Rep gene;

the mutations in the comprise replacements of native amino acid residue(s), wherein the replacing amino acid is other than an alanine;

the AAV serotype is an AAV-1, AAV-2, AAV-3, AAV-3b, AAV-4 or AAV6 serotype; and

the mutation is in the corresponding position in each serotype.

106. (New) An isolated cell, comprising the nucleic acid molecule of claim 105.

107. (New) A recombinant AAV, comprising the nucleic acid molecule of claim 105.

108. (New) A nucleic acid molecule that encodes a mutant adeno-associated virus (AAV) Rep protein that has increased activity, wherein:

the mutant is not a temperature-sensitive mutation;

increased activity of the Rep protein is manifested as an increased titer of virus upon introduction and replication of the virus in a host cell that contains in its genome the nucleic acid molecule encoding the mutant Rep protein, compared to the titer of virus upon introduction and replication of a virus in a host cell containing a wild type Rep gene;

the mutations in the comprise replacements of native amino acid residue(s), wherein the replacing amino acid is other than an alanine;

the AAV serotype is an AAV-1, AAV-2, AAV-3, AAV-3b, AAV-4 or AAV6 serotype; and

the mutation is in the corresponding position in each serotype.

109. (New) An isolated cell, comprising the nucleic acid molecule of claim 108.

110. (New) A recombinant AAV, comprising the nucleic acid molecule of claim 108.